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LETTER

## Heat therapy: an ancient concept re-examined in the era of advanced biomedical technologies

The effect of passive heat therapy on vascular mechanical and functional properties reported in *The Journal of Physiology* in the study of Brunt *et al.* (2016) could be a substantial mechanism contributing to the observed reduction of cardiovascular-related and all-cause mortality after long-term sauna bathing (Laukkanen *et al.* 2015).

Several favourable effects of heat therapy have been known since antiquity. In the fifth century BC Hippocrates (460–377 BC) noted that malarial fever could have a calming effect in epileptics 'febrem convulsioni supervenire melius est, quam convulsionem febri', in other words 'fever resolves spasm' (Marks, 1817), while the Roman encyclopaedist Aulus Cornelius Celsus (25 BC–AD 50) suggested for the treatment of dropsy (oedema) heated sand and warm baths (Adams, 1834). Thermothererapy passed on the treatment of psychiatric disorders in the 19th century as it is mentioned in the work of the famous French psychiatrist Philippe Pinel (1745–1826) (Pinel, 1801). However the 'capping stone' of thermotherapy occurred at the beginning of the 20th century, in the pre-penicillin era, when the Austrian psychiatrist Julius Wagner-Jauregg (1857–1940) received the Nobel Prize in Medicine and Physiology in 1927 for his work on the therapeutic value of fever therapy in the treatment of neurosyphilis (Karamanou *et al.* 2013).

Today, the advances in medical technology offer a plethora of diagnostic tools for the assessment and quantification of cardiovascular properties, allowing us to explore the mechanisms beyond the beneficial effects of heat therapy on the cardiovascular system. However, this plethora of different methods and devices requires the use of validated and standardized procedures so as to provide accurate, reproducible, comparable and clinically meaningful measurements.

We would like to comment on methods assessing arterial stiffness, which is an emerging established vascular biomarker and which, beyond its physiological relevance regarding the optimal vascular function and a balanced ventriculo-arterial coupling, is a strong and independent predictor of cardiovascular risk and mortality (Vlachopoulos *et al.* 2010; Ben-Shlomo *et al.* 2014).

A few methodological issues concerning the assessment of arterial stiffness should be further clarified concerning the study of Brunt *et al.* (2016). The measurement of carotid-to-femoral pulse wave velocity (cf-PWV) (gold-standard for the assessment of arterial stiffness) depends on several methodological parameters that may affect its accuracy and precision, with a direct impact on the clinical interpretation of the measured values. For this reason, existing guidelines and expert consensus documents recommend specific procedures and techniques for cf-PWV measurement. Two major parameters are (a) the distance between the two recording sites and (b) the transit time (TT) of the pressure wave travelling from the carotid to the femoral artery. As regards the distance measurement in the study of Brunt *et al.* (2016), the direct length between the two recording sites was used. However, we should note that recent expert consensus documents and guidelines advised that the distance should be calculated by multiplying the direct distance by 0.8 (Van Bortel *et al.* 2012), while others support that the subtracted distance (suprasternal notch to common femoral artery minus suprasternal notch to common carotid artery) is more anatomically relevant (Townsend *et al.* 2015).

Concerning the TT, it is evident that several foot-to-foot algorithms exist for its estimation, which, however, may result in different calculations of variable accuracy and precision (Millasseau *et al.* 2005; Vardoulis *et al.* 2013). Brunt and colleagues used the 'upswing of the pressure tracing' (Brunt *et al.* 2016) in order to estimate TT. Previous *in vivo* and an *in silico* studies have shown that the first derivative method consistently provides less accurate and less precise estimations whereas the tangential (or intersecting tangents) method has been found to be more appropriate and robust for TT estimation (Chiu *et al.* 1991; Vardoulis *et al.* 2013).

Finally, the number of cf-PWV measurements performed in each session in this study is not clear, but it is a critical methodological prerequisite. It has been reported that substantial differences may be observed between two repeated measurements of cf-PWV (Papaioannou *et al.* 2012), even if each cf-PWV value is derived from several sequential pulse waves. Hence, it is recommended to perform at least two measurements and if their difference is greater than 0.5 m $s^{-1}$, then a third measurement should be performed and the median value should be used (Van Bortel *et al.* 2012; Townsend *et al.* 2015).

Brunt *et al.* found that passive heat therapy can cause an average reduction of cf-PWV of 1 m $s^{-1}$, in 10 healthy young subjects (from 7.1 ± 0.3 to 6.1 ± 0.3 m $s^{-1}$). It should be further addressed that this is a remarkable reduction which corresponds to an approximate 15% decrease in cardiovascular risk and mortality (Vlachopoulos *et al.* 2010). Of note, reduction of pressure wave reflections as well as a favourable decrease in aortic blood pressure and increase in pulse pressure amplification – not evaluated in the present study – are also anticipated as a consequence of arterial stiffness reduction and potential decrease in wave reflections coefficients due to vasodilation. These effects merit further investigation.

Undoubtedly, this study provides important evidence regarding the beneficial physiological effects of heat on vascular properties (both functional and structural), but the exact mechanisms through which these properties are influenced by long-term passive heat therapy remain unclarified.

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